

CLAIMS

We claim:

1. The use of a set of at least one meal, at least one meal of said set comprising at least one constituent operative to cause retention of said at least one meal in the stomach of a subject, and having a predetermined volume, for determination of gastric accommodation of the subject by means of at least two measurements of a gastric emptying parameter of said at least one meal as a function of the volume of said meal having exited the stomach of the subject.
2. The use of a set of at least one meal according to claim 1 wherein said at least one meal is one meal, and said at least two measurements are performed on said one meal.
3. The use of a set of at least one meal according to claim 3 wherein at least one of said at least two measurements is performed on a liquid emptying phase of said meal from the stomach of the subject.
4. The use of a set of at least one meal according to claim 1 wherein said at least one meal is at least two meals, and one of said at least two measurements is performed on a first one of said at least two meals, and a second one of said at least two measurements is performed on a second one of said at least two meals.
5. The use of a set of two meals according to claim 4 wherein said first one of said at least two meals is larger than the second one of said at least two meals.
6. The use of a set of two meals according to claim 4 wherein said second one of said at least two meals is larger than the first one of said at least two meals.

7. The use of a set of at least two meals according to claim 6 wherein said second one of said at least two meals is at least twice as large as said first one of said at least two meals.

8. The use of a set of at least one meal according to any of claims 1 to 7 wherein said predetermined volume is at least 150 milliliters.

9. The use of a set of at least one meal according to any of claims 1 to 7 wherein at least one meal of said set comprises a marker which is detected after leaving the stomach of said subject.

10. The use of a set of at least one meal according to claim 9 and wherein said marker is detected by its presence in the exhaled breath of said subject.

11. The use of a set of at least one meal according to claim 9 and wherein said marker is detected by its presence within the body of said subject.

12. The use of a set of at least one meal according to claim 11 and wherein said marker is detected by its presence in the gastro-intestinal tract of said subject.

13. The use of a set of at least one meal according to any of claims 1 to 12, wherein at least one meal of said set comprises at least one of:

- a caloric value of at least 150 kcalories;
- a lipid content of at least 5 %;
- a carbohydrate content of at least 10 %;
- a protein content of at least 5%; and
- a pH value of less than 3.

14. The use of a set of at least one meal according to claim 13 wherein said carbohydrate is glucose.

15. A single-dosage liquid meal for use by a subject in a breath test, comprising;

- a volume of at least 500 milliliters;
- an agent causing gastric retention of said meal; and
- a marker, stable in the gastric environment, and detectable upon exiting the stomach of the subject.

16. A single-dosage liquid meal according to claim 15, wherein said agent comprises at least one of:

- a caloric value of at least 150 kcalories,
- a lipid content of at least 5 %;
- a carbohydrate content of at least 10 %;
- a protein content of at least 5%; and
- a pH value of less than 3.

17. Apparatus for determining the gastric accommodation of a subject, following sequential administration to the subject of a first and a second meal, at least one of said meals comprising a marker detectable upon exiting the stomach of the subject, said apparatus comprising:

- a detector for detecting said marker upon exiting the stomach of said subject, and providing a marker output signal conveying information about the rate of emptying of said meal from the stomach of the subject; and

- a data processing system receiving said marker output signal and calculating a first set of parameters which characterizes the gastric emptying of said first meal, and a second corresponding set of parameters which characterizes the gastric emptying of said second meal, and which determines said gastric accommodation by comparing two corresponding parameters from said first and said second sets of parameters.

18. Apparatus according to claim 17 and wherein said first and said second meals are of different volumes.

19. Apparatus according to claim 18 and wherein said gastric accommodation is determined from the dependence of said parameters on the volumes of said first and second meals.

20. Apparatus according to claim 17 and wherein said first and said second meals are of similar volumes, and said second meal is administered before said first meal has emptied from the stomach of the subject.

21. Apparatus according to any of claims 17 to 20, wherein said processing system compares a set of parameters of said second meal before said first meal has emptied from the stomach of said subject.

22. Apparatus according to any of claims 17 to 21 and wherein said marker is detected by its presence in the exhaled breath of said subject.

23. Apparatus according to any of claims 17 to 21 and wherein said marker is detected by its presence within the body of said subject.

24. Apparatus according to claim 23 and wherein said marker is detected by its presence in the gastro-intestinal tract of said subject.

25. Apparatus according to any of claims 17 to 24, wherein said set of parameters comprises at least one of:

$t_{\frac{1}{2}}$;

t_{lag} ;

GEC;

CPDR; and

the integral under a plot of the DoB as a function of time.

26. A kit for the diagnosis of gastric accommodation in a subject, comprising:

a quantity of material for marking a first meal having a first predetermined volume and a first predetermined gastric retention characteristic;

a quantity of material for marking a second meal having a second predetermined volume and a second predetermined gastric retention characteristic; and

a protocol providing information relating to the preparation of said first meal and of said second meal.

27. The kit of claim 26, and wherein said protocol also provides information relating to the administration of said first and said second meals to the subject.

28. The kit of claim 27, and wherein said protocol also provides information relating to the point in time when said second meal is taken, according to the results of gastric emptying measured on said first meal.

29. A kit for the diagnosis of gastric accommodation in a subject according to claim 26, and also comprising material for the preparation of at least one of said first and said second meals.

30. A kit for the diagnosis of gastric accommodation in a subject according to claim 26, and also comprising a breath collecting device.

31. Breath test apparatus for determining at least one gastro-intestinal condition in a subject, comprising:

a breath collection device for collecting breath from a subject after ingestion of a marked substrate; and

a gas analyzer for detecting the products of said marked substrate in the exhaled breath of said subject;

wherein said breath test apparatus and said marked substrate are adapted to perform a first breath test selected from a group of possible breath tests providing gastro-intestinal information related to said subject;

and wherein said breath test apparatus and said marked substrate are also adapted to perform at least a second breath test selected from said group of breath

tests, according to the outcome of at least said first breath test, such that a gastro-intestinal condition of said subject is determined from the outcome of at least one of said breath tests.

32. The apparatus of claim 31 and wherein said gastro-intestinal condition comprises at least one of dyspepsia and irritable bowel syndrome.

33. The apparatus of claim 32 and wherein said dyspepsia arises from at least one of a gastric emptying disorder, a gastric accommodation disorder, and a *Helicobacter pylori* infection.

34. The apparatus of claim 32 and wherein said irritable bowel syndrome arises from at least one of a sugar malabsorption disorder, a bacterial overgrowth, and an orocecal transit time disorder.

35. The apparatus of claim 34 and wherein said sugar malabsorption disorder is at least one of lactose intolerance, fructose intolerance, sucrose intolerance and maltose intolerance.

36. Breath test apparatus for the determination of gastric emptying of a subject, comprising:

a gas collector, for collecting exhaled breath samples from the subject after administration of a test meal comprising a marker, whose by-products are exhaled in said breaths of said subject in accordance with the rate of emptying of said marker from the stomach of said subject;

a gas analyzer for analyzing said collected exhaled breath, wherein said analyzing is performed essentially continuously; and

a computing system which calculates, as the breath test proceeds, at least one of the $t_{1/2}$, t_{lag} , delta over baseline (DoB)curve amplitude, the integral under the plot of the DoB as a function of time, and Gastric Emptying Coefficient (GEC) parameters of said subject;

wherein said breath test apparatus provides an indication of a gastric emptying disorder by determining a final estimated value of at least one of said parameters, and determining whether said parameter departs significantly from known norms for the value of said parameter.

37. The apparatus according to claim 36, and wherein an indication is provided of a gastric emptying disorder in said subject while said subject is still providing breath samples to said analyzer.

38. The apparatus according to claim 36, and wherein an indication is provided of a gastric emptying disorder in said subject in accordance with the on-going analyses of said breaths of said subject.

39. A substrate for isotopic breath tests, comprising an isotopically labeled material in a micro-encapsulated coating material, wherein the properties of the micro-encapsulation coating material are chosen such that said isotopically labeled material is released in a predetermined part of the gastro-intestinal tract.

40. The substrate according to claim 39 and wherein said micro-encapsulation coating material is chosen such that it breaks down and releases the isotopically labeled material according to the pH value of the environment through which it is passing.

41. The substrate according to claim 40 and wherein said micro-encapsulation coating material is chosen such that it breaks down and releases the isotopically labeled material only after leaving the stomach of a subject.

42. The substrate according to claim 41 and wherein said isotopically labeled material is used as a marker for determining passage through the duodenum.

43. The substrate according to claim 39 and wherein said micro-encapsulation coating material is chosen such that it breaks down and releases the isotopically

labeled material under the effect of enzymic action arising from the enzymic environment through which it is passing.

44. The substrate according to claim 43 and wherein said enzymes are those secreted by at least one of the pancreas and the gall bladder, such that said isotopically labeled material is used as a marker for determining passage through the duodenum.

45. The substrate according to claim 39 and wherein said micro-encapsulation coating is such that it can be more readily bonded to an administered meal than said isotopically labeled material.

46. The use of a set of a first and a second liquid meal in determining the gastric accommodation of a subject, said first liquid meal comprising a first predetermined volume, and said second liquid meal comprising a second predetermined volume greater than the first predetermined volume and having a predetermined gastric retention characteristic;

wherein said second liquid meal is administered to the subject after said first liquid meal has begun emptying from the stomach of the subject; and

wherein the gastric accommodation of the subject is determined according to the deviation between a measured rate of emptying of said second meal and a measured rate of emptying of said first meal.

47. The use of a set of meals according to claim 46 and wherein said second predetermined volume is sufficient to cause gastric distension in said subject.

48. The use of a set of meals according to claim 46 and wherein said second predetermined volume is at least 500 milliliters of liquid.

49. The use of a set of meals according to claim 46 and wherein said gastric retention characteristic arises from at least one of a predetermined pH, a

predetermined calorific value and a predetermined composition of said second liquid meal.

50. The use of a set of meals according to claim 49 and wherein said predetermined pH is less than 3.0.

51. The use of a set of meals according to claim 49 and wherein said predetermined calorific value is at least 150 kilocalories.

52. The use of a set of meals according to claim 49 and wherein said predetermined composition is an isotonic composition.

53. The use of a set of meals according to claim 46 and wherein said second liquid meal is administered as soon as said rate of emptying of said first meal from the stomach of the subject is determined.

54. The use of a set of meals according to claim 46 and wherein said second liquid meal is administered after a time when essentially all physiological effects of said first meal on the subject have terminated.

55. The use of a set of meals according to claim 54 and wherein said second liquid meal is administered on a successive day to said first meal.

56. The use of a set of meals according to any of claims 46 to 55, wherein said rate of emptying is determined by one of a breath test, scintigraphy, an X-ray, computerized tomography, gamma imaging and an ultrasound method.

57. The use of a liquid meal comprising a predetermined volume and having a predetermined gastric retention characteristic, in determining the gastric accommodation of a subject;

wherein the average gastric emptying rate of said meal for a large plurality of normal subjects is known;

and wherein the rate of emptying of said meal from the stomach of the subject is measured;

and wherein the deviation between said rate of emptying of said meal from the stomach of the subject and said average rate of emptying of said meal for a large plurality of normal subjects, provides an indication of the gastric accommodation of the subject.

58. The use of a liquid meal according to claim 57 and wherein said predetermined volume is sufficient to cause gastric distension in said subject.

59. The use of a liquid meal according to claim 57 and wherein said predetermined volume is at least 500 milliliters of liquid.

60. The use of a liquid meal according to claim 57 and wherein said gastric retention characteristic arises from at least one of a predetermined pH, a predetermined calorific value and a predetermined composition of said liquid meal.

61. The use of a liquid meal according to claim 60 and wherein said predetermined pH is less than 3.0.

62. The use of a liquid meal according to claim 61 and wherein said predetermined calorific value is at least 150 kilocalories.

63. The use of a liquid meal according to claim 61 and wherein said predetermined composition is an isotonic composition.

64. The use of a liquid meal according to any of claims 57 to 63, wherein said rate of emptying is determined by one of a breath test, scintigraphy, an X-ray, computerized tomography, gamma imaging and an ultrasound method.

65. The use of an isotopically labeled liquid meal, comprising a predetermined volume and having a predetermined gastric retention characteristic, for determining the effect of the volume of a meal on the intragastric pressure of a subject;

wherein the rate of emptying of said meal from the stomach of the subject is determined by means of a breath test performed to detect isotopically labeled products of said meal in the breath of the subject, for meals of varying predetermined volumes.

66. The use of a meal administered to a subject, for the determination of gastro-intestinal disorders in the subject, said meal comprising at least a first and a second marker material, said first material being such that it is not generally absorbed in the subject's stomach, and releases a predefined gas in the presence of intestinal bacteria, and said second material being such that it indicates a location of said meal within the gastro-intestinal tract of the subject;

wherein the generation of said predefined gas in said subject is detected by means of a breath test, and the position within the subject's gastro-intestinal tract at which said predefined gas is generated is determined by means of said second marker material.

67. The use of a meal according to claim 66, and wherein a by-product of said second marker material is also detected by means of a breath test, such that the position of said predefined gas generation in the gastro-intestinal tract of said subject is determined by the temporal relationship between the appearance of said predefined gas and of a by-product of said marker material in said subject's breath.

68. The use of a meal according to claim 67, and wherein said second marker material is labeled with a carbon isotope, and said by-product is isotopically labeled carbon dioxide.

69. The use of a meal according to any of claims 66 to 68, and wherein said first material is a sugar metabolized in the small intestine of said subject, such that the time of detection of said predefined gas relative to the time of detection of the

second marker material is used to determine the presence of bacterial overgrowth in said small intestine.

70. The use of a meal according to claim 69, and wherein said second material is a labeled sugar also metabolized in the small intestine of said subject, such that the generally concurrent appearance in the breath of said subject of said predefined gas and a by-product of said second marker material is indicative of the presence of bacterial overgrowth in said subject.

71. The use of a meal according to claim 69, and wherein said second material is a labeled sugar also metabolized in the small intestine of said subject, such that the appearance in the breath of said subject of a by-product of said second marker material significantly prior to the appearance of said predefined gas is generally indicative of the absence of bacterial overgrowth in said subject.

72. The use of a meal according to any of claims 69 to 71 and wherein said first material is at least one of glucose and lactulose.

73. The use of a meal according to claim 69, and wherein said second material is at least one of labeled sodium acetate, sodium octanoate, glucose, an acetyl leucine probe, or a microencapsulated labeled substrate

74. The use of a use of a meal according to any of claims 66 to 68, and wherein said first material is a sugar generally metabolized in the small intestine of said subject, such that detection of said predefined gas essentially concurrent with detection of a small quantity of said second marker material is used to determine the orocaecal transit time of said subject.

75. The use of a meal according to any of claims 66 to 68, and wherein said first material is a sugar of a group thought to be malabsorbed in the small intestine of said subject, such that it arrives essentially unabsorbed at the colon of said subject, where said predefined gas is generated by the presence of colonic bacteria, such that

the time of detection of said predefined gas relative to the time of detection of the second marker material is used to determine a sugar intolerance in said subject.

76. The use of a meal according to claim 75, and wherein said second material is an isotopically labeled material generally absorbed in the colon, such that detection of said predefined gas essentially concurrent with detection of labeled by-products of said second marker material is used to determine a sugar intolerance in said subject.

77. The use of a meal according to claim 76, and wherein said second material is xylose labeled with a carbon isotope, and said by-product is isotopically labeled carbon dioxide.

78. The use of a meal according to claim 75, and wherein said second material is an isotopically labeled material generally absorbed in the small intestine, such that the relative time and quantity of detection of said predefined gas and labeled by-products of said second marker material is used to determine whether said subject is suffering from one or both of a sugar intolerance and a bacterial overgrowth.

79. The use of a meal according to claim 78, and wherein the detection of a small quantity of said predefined gas, characteristic of a small part of said first material in the presence of bacteria, occurring essentially concurrently with the detection of said labeled by-products of said second marker material indicates that said subject is suffering a bacterial overgrowth.

80. The use of a meal according to claim 78, and wherein the detection of said predefined gas later than the detection of said labeled by-products of said second marker material indicates that said subject is suffering from a sugar intolerance.

81. The use of a meal according to claim 78, and wherein the detection of a large quantity of said predefined gas, characteristic of the majority of said first material in the presence of bacteria, occurring essentially concurrently with the detection of said

labeled by-products of said second marker material indicates that said subject is suffering a sugar intolerance and a bacterial overgrowth.

82. The use of a meal according to any of claims 75 to 81, and wherein said sugar is at least one of the group consisting of lactose, fructose, maltose and sucrose.

83. The use of a meal according to any of claims 66 to 82, and wherein said predefined gas is at least one of hydrogen and methane.

84. Breath test apparatus comprising:

a breath sample input port for receiving exhaled breath from a subject after administration to the subject of at least one meal, at least one of said at least one meal comprising a marker detectable upon exiting the stomach of the subject;

at least one gas analyzer for detecting said marker in the exhaled breath of the subject;

a gastric function processing module, receiving information from said at least one gas analyzer and determining at least one of the gastric emptying rate and the gastric accommodation of the subject;

dyspeptic symptom input functionality, receiving information from the subject about the level of dyspeptic symptoms perceived at least upon administration of said first meal and said second meal; and

a gastro-intestinal diagnostic processor, receiving information from said gastric function processing module and said dyspeptic symptom input functionality, and providing an output indicative of the visceral sensitivity of the subject.

85. Breath test apparatus according to claim 84, and wherein said at least one meal comprises at least a first and a second meal, at least one of said meals comprising a marker detectable upon exiting the stomach of the subject

86. Breath test apparatus comprising:

a breath sample input port for receiving exhaled breath from a subject after administration to the subject of at least one meal, at least one of said at least one meal comprising a marker detectable upon exiting the stomach of the subject;

at least one gas analyzer for detecting said marker in the exhaled breath of the subject;

a gastric function processing module, receiving information from said at least one gas analyzer and determining the gastric emptying rate and the gastric accommodation of the subject; and

a gastro-intestinal diagnostic processor, receiving information from said gastric function processing module and providing an evaluation of at least two causes of functional gastro-intestinal disorders in a single procedure.

87. Breath test apparatus according to claim 86, and wherein said at least one meal comprises at least a first and a second meal, at least one of said meals comprising a marker detectable upon exiting the stomach of the subject

88. Breath test apparatus comprising:

a breath sample input port for receiving breath from a subject after administration to the subject of at least one meal, at least one of said at least one meal comprising a marker detectable upon exiting the stomach of the subject;

at least one gas analyzer for detecting said marker in the exhaled breath of the subject;

a gastric function processing module, receiving information from said at least one gas analyzer and determining at least one of gastric emptying rate and gastric accommodation of the subject;

dyspeptic symptom input functionality, receiving information from the subject about the level of dyspeptic symptoms perceived at least upon administration of said first meal and said second meal; and

a gastro-intestinal diagnostic processor, receiving information from said gastric function processing module and said dyspeptic symptom input functionality, and providing an evaluation of at least one cause of dyspepsia in a

subject, said at least one cause being selected from gastric accommodation, gastric emptying and visceral sensitivity, in a single procedure.

89. Breath test apparatus according to claim 88, and wherein said at least one meal comprises at least a first and a second meal, at least one of said meals comprising a marker detectable upon exiting the stomach of the subject

90. A kit for use in a breath test for the evaluation of at least one of the causes of dyspepsia in a subject, comprising:

a first quantity of material for marking a first meal having a first predetermined volume and a first predetermined gastric retention characteristic;

a second quantity of material for marking a second meal having a second predetermined volume and a second predetermined gastric retention characteristic; and

a protocol providing information relating to the preparation of said first meal and of said second meal,

wherein said breath test evaluates at least one of the causes of dyspepsia in a subject selected from gastric accommodation, gastric emptying and visceral sensitivity in a single procedure.

91. The kit of claim 90, and wherein said first predetermined volume and said second predetermined volume are different.

92. The use of a set of a first and a second meal in determining at least two of gastric accommodation, gastric emptying and visceral sensitivity of a subject, said first meal comprising a first predetermined volume, and said second liquid meal comprising a second predetermined volume and having a second predetermined gastric retention characteristic;

wherein said second meal is administered to the subject after said first liquid meal has begun emptying from the stomach of the subject; and

wherein the measured emptying rates of said first and second meal are utilized to determine the gastric emptying and gastric accommodation level of said subject; and

wherein dyspeptic symptoms of the subject are ascertained at least upon administration of said first and said second meal; and

wherein said dyspeptic symptoms of the subject are correlated with the volumes of said first and second meal to determine the level of visceral sensitivity, such that at least two of gastric accommodation, gastric emptying and visceral sensitivity of a subject may be determined in a single procedure.

93. The use of a set of meals according to claim 92, and wherein said first predetermined volume and said second predetermined volume are different.

94. The use of a set of at least one meal, at least one meal of said set comprising at least one constituent operative to cause retention of said at least one meal in the stomach of a subject, and having a predetermined volume, for determination of at least two of gastric accommodation, gastric emptying and visceral sensitivity of a subject,

wherein said gastric accommodation and said gastric emptying are determined by making at least two measurements of a gastric emptying parameter of said at least one meal as a function of the volume of said meal having exited the stomach of the subject, and

wherein dyspeptic symptoms of the subject are ascertained as a function of the volume of said meal retained in the stomach of the subject to determine the level of visceral sensitivity, such that at least two of gastric accommodation, gastric emptying and visceral sensitivity of a subject may be determined in a single procedure.

95. The use of a set of at least one meal, according to claim 94, and wherein said first predetermined volume and said second predetermined volume are different.

96. The use of a set of at least a first and a second meal in making an evaluation of at least two causes of functional gastro-intestinal disorders in a single procedure said first meal comprising a first predetermined volume and having a first predetermined gastric retention characteristic, and said second liquid meal comprising a second predetermined volume and having a second predetermined gastric retention characteristic;

wherein said second meal is administered to the subject after said first liquid meal has begun emptying from the stomach of the subject; and

wherein the measured gastric emptying rates of said first and second meal are utilized to determine the gastric accommodation of said subject, such that an evaluation of at least two causes of functional gastro-intestinal disorders can be made in a single procedure.

97. The use of a set of at least one meal in making an evaluation of at least two causes of functional gastro-intestinal disorders in a single procedure, said at least one meal comprising a predetermined volume, and having a predetermined gastric retention characteristic;

wherein at least two measurements of the gastric emptying rate of said at least one meal are performed as a function of the volume of said meal having exited the stomach of the subject; and

wherein said at least two measurements are utilized to determine the gastric accommodation of said subject, such that an evaluation of at least two causes of functional gastro-intestinal disorders can be made in a single procedure.

98. The use of a set of at least a first and a second meal in providing an indication of the visceral sensitivity of a subject, said first meal comprising a first predetermined volume and having a first predetermined gastric retention characteristic, and said second liquid meal comprising a second predetermined volume and having a second predetermined gastric retention characteristic;

wherein said second meal is administered to the subject after said first liquid meal has begun emptying from the stomach of the subject; and

wherein the measured gastric emptying rates of said first and second meal are utilized to determine the gastric accommodation of said subject, such that the gastric emptying and the gastric accommodation of the subject are known; and

wherein information is provided by the subject about the level of dyspeptic symptoms perceived at least upon administration of said first meal and said second meal, said information being correlated with said gastric emptying and gastric accommodation of the subject by means of a gastro-intestinal diagnostic processor, such that an output indicative of the visceral sensitivity of the subject is obtained.

99. The use of a set of at least one meal in providing an indication of the visceral sensitivity of a subject, said at least one meal comprising a predetermined volume, and having a predetermined gastric retention characteristic;

wherein at least two measurements of the gastric emptying rate of said at least one meal are performed as a function of the volume of said meal having exited the stomach of the subject; and

wherein said at least two measurements are utilized to determine the gastric accommodation of said subject, such that the gastric emptying and the gastric accommodation of the subject are known; and

wherein dyspeptic symptoms of the subject are ascertained as a function of the volume of said meal retained in the stomach of the subject, said information being correlated with said gastric emptying and gastric accommodation of the subject by means of a gastro-intestinal diagnostic processor, such that an output indicative of the visceral sensitivity of the subject is obtained.